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The role of chest tomography in the diagnosis of COVID-19

COVID-19 tanısında göğüs tomografisinin rolü

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ABSTRACT

Aim: We aimed to examine the diagnostic power of chest computerized tomography (CT) comparing with 'Clinical Decision' and RT-PCR results among the patients admitted to the hospital with COVID-19 disease suspicion.

Material and Method: This study included 162 patients who applied to the pandemic outpatient clinic between March 11 and April 11, 2020, suspected of new coronavirus infection, and had chest CT and RT-PCR tests at the same time. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), accuracy and positive odds ratio of RT-PCR and chest CT imaging are investigated for the diagnosis of COVID-19.

Results: It was found that 56.8% (92 patients) of chest CT scans taken at admission were compatible with viral pneumonia. With the 'Clinical Decision', which we accept as the gold standard diagnostic method, 61.1% of the patients (99 patients) were evaluated as COVID-19 positive and treatment was started. According to clinical decision, sensitivity of chest CT was 92.9%.

Conclusion: COVID-19 pneumonia is a serious life-threatening condition. Rapid diagnosis and early treatment are very important in terms of reducing mortality and morbidity. The chest CT might create an early diagnosis and treatment opportunity.

Keywords: COVID-19, coronavirus, pneumonia, chest, computerized tomography

ÖZ

Amaç: COVID-19 hastalığı şüphesiyle hastaneye başvuran hastalarda göğüs bilgisayarlı tomografi (BT)'sinin 'Klinik Karar' ve RT-PCR sonuçları ile karşılaştırmalı olarak tanısal gücünü incelemeyi amaçladık.

Gereç ve Yöntem: Bu çalışmaya 11 Mart - 11 Nisan 2020 tarihleri arasında pandemi polikliniğine başvuran, yeni koronavirüs enfeksiyonu şüphesi olan ve aynı anda göğüs BT ve RT-PCR tetkikleri yapılan 162 hasta dahil edildi. COVID-19 tanısı için RT-PCR ve göğüs BT görüntülemenin duyarlılığı, özgüllüğü, pozitif öngörü değeri (PPV), negatif öngörü değeri (NPV), doğruluğu ve pozitif olasılık oranı araştırılmaktadır.

Bulgular: Başvuru sırasında çekilen akciğer tomografilerinin %56,8'inin (92 hasta) viral pnömoni ile uyumlu olduğu bulundu. Altın standart tanı yöntemi olarak kabul ettiğimiz 'Klinik Karar' ile hastaların %61,1'i (99 hasta) COVID-19 pozitif olarak değerlendirildi ve tedaviye başlandı. Klinik karara göre göğüs BT'nin duyarlılığı %92,9 idi.

Sonuç: COVID-19 pnömonisi hayatı tehdit eden ciddi bir durumdur. Hızlı tanı ve erken tedavi, mortalite ve morbiditeyi azaltmak açısından çok önemlidir. Göğüs BT erken tanı ve tedavi fırsatı yaratabilir.

Anahtar Kelimeler: COVID-19, coronavirüs, pnömoni, göğüs, bilgisayarlı tomografi

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INTRODUCTION

COVID-19 infection can occur in a wide spectrum of asymptomatic disease, mild upper respiratory tract infection, respiratory failure and severe viral pneumonia that can result in death (1). The most common symptoms are nonspecific findings such as shortness of breath, cough, fever, headache, muscleaches and weakness (2). Approximately 20% of cases are severe and mortality is about %3 (3).

Since there is no specific treatment for COVID-19, it is important to detect infected people early and isolate them from the healthy population. In the differential diagnosis of COVID-19 pneumonia, imaging tests should also be used in addition to the patient's history, clinical, laboratory findings and coronavirus specific diagnostic tests (4). In literature, the diagnostic value of chest x-ray is relatively low as 30–60% in COVID-19 pneumonia. Although it is possible to see some abnormalities in viral pneumonia on chest x-rays, it cannot be excluded the disease if the chest x-ray is normal (5). Non contrast chest computed tomography (CT) should be considered for early diagnosis of viral disease in suspected patients with normal chest x-ray (6).

RT-PCR means that many COVID-19 patients can not be detected at the first admission and can not receive appropriate treatment on time. Such patients pose a risk to infect a larger population, given the highly infectious nature of the virus (7). Chest CT, a routine thorax imaging tool for the diagnosis of pneumonia, is a relatively easy and fast imaging method. Typical chest CT radiographic features in almost all COVID-19 patients are pathchy subpleural ground glass densities, multifocal irregular consolidation and / or interstitial changes with peripheral distribution (**Figure 1**) (8,9). These typical radiological findings have also been observed in patients with negative RT-PCR results, but with clinical symptoms (10).

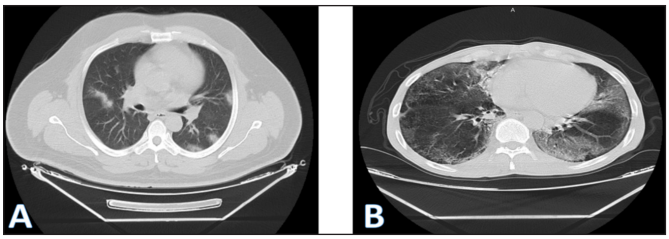

Figure 1. Chest CT image. **A.** Chest CT image of a 48-years-old RT-PCR negative male patient; irregular subpelural nodular infiltrations **B.** Chest CT image of a 45-years-old RT-PCR negative male patient; subpleural groundglass infiltrations with crazy paving in lower and middle zones

In this study, we aimed to examine the diagnostic power of chest CT by expert compatibility and RT-PCR in 162 patients admitted to the hospital with suspicion of COVID-19.

MATERIAL AND METHOD

The study was carried out with the permission of Yıldırım Beyazıt University Faculty of Medicine Clinical Research Ethics Committee (Date; 09.09.2020, Decision No: 72). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Patients and Study Design

The study included 162 patients who applied to the pandemic outpatient clinics between March 11 and April 11, 2020, suspected of new coronavirus infection, and had chest CT and RT-PCR tests at the same time. Because our study was retrospective, informed consent was not obtained.

Patients over 18 years of age who applied to the COVID polyclinic and underwent chest CT scan and nasopharyngeal swab RT-PCR were included in this study. Patients under the age of 18 were excluded from the study.

Especially in patients with COVID-19 pneumonia, advanced age and comorbidity require rapid diagnosis and treatment. False negative results and late diagnosis may be fatal in these patients. In patients with negative RT-PCR tests, 1 pulmonologist (MD), 2 infectious diseases specialists (TUU, SSG) and 1 radiologist (MEA) experienced in the field of all patients to identify COVID-19 with higher sensitivity blindly evaluated by RT-PCR test results. All physicians had access to patients' exposure history, clinical symptoms, and CT images. Regardless of RT-PCR results, patients were reported as COVID-19 compatible or not with expert opinion. Considering the rapidly spreading COVID-19 epidemic with Clinical Decision, our aim in our study was to detect especially mortal COVID-19 pneumonias, isolate patients and apply appropriate treatment quickly.

The Chest CT Assessment

Chest CT examinations were performed using a 16-channel multi-detector CT device (GE Brightspeed). CT specification: tubevoltage, 120 kVp; tubecurrent, standard (reference mAs, 80–180); slicethickness, 1.25 mm; reconstructionrange is 0,625 mm. All chest CT images were obtained with full inspiration in the patient's supine position and without contrast material. All chest CT evaluation performed by an experienced radiologist.

RT-PCR test

The COVID-19 respiratory samples in patients matching to the probable case definition of SARS-CoV-2 has been evaluated by Turkey General Directorate of Public Health (GDPH) Microbiology Reference Laboratory. Nucleic acid amplification tests (NAAT) for SARS-CoV-2 virus and routine confirmation of COVID-19 cases based

on detection of specific sequences of virus RNA with a NAAT test such as real-time reverse transcription-polymerase chain reaction (rRT-PCR) and when necessary verification by sequence analysis method.

Statistical Analysis

As a result of post-hoc power analysis, the power calculated by considering the frequency of diagnosis with both tests (57% vs 22%) was found to be 100% at a confidence interval of 95%.

Statistical Package for Social Sciences (SPSS), version 22.0 (SPSS Inc. Chicago, USA) computer package program was used for statistical analysis of the research data.

Categorical variables were shown as numbers and percentages, and continuous variables were presented with mean±standard deviation (SD) and median (min-max) for descriptive analysis. A Chi-square test was used in comparison analysis for categorical variables.

In this study, the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), accuracy and positive probability ratio of the RT-PCR, and chest CT imaging in the application to diagnose COVID-19 were presented. In addition, the consistency of both tests according to the expert opinion is presented with the value of kappa and its p-value. Consistency between observations for CT and RT-PCR was evaluated with the kappa value and its p-value.

RESULTS

One hundred sixty two COVID-19 suspicious patients with an average age of 48.42 ±17.98 (range 18-90) years were included in the study. 23,5% (38 patients) of the patients are 65 years and older, 54,9%(89 patients) are male. It was found that 56,8% (92 patients) of the chest CT obtained up on admission were compatible with viral pneumonia (**Table 1**).

Table 1. Baseline demografics

Age, year	
Mean±sd	48.42 ±17.98
Median (min-max)	46.0 (18-90)
Age, n (%)	
<65 years	124 (76.5)
≥65 years	38 (23.5)
Sex, n (%)	
Female	73 (45.1)
Male	89 (54.9)
Chest CT scan, n (%)	
Consistent with viral pneumonia (positive)	92 (56.8)
No CT findings of viral pneumonia	70 (43.2)
Clinical decision, n (%)	
COVID-19 positive	99 (61.1)
COVID-19 negative	63 (38.9)

Thoracic ground glass density/consolidation, multifocal opacities were observed in the early period (after the onset of symptoms, days 0-4). In the interim period (days 5-13), new progressive consolidation and bilateral-multi lobar involvement were observed. Regression of late period (>14 days) lesions were detected, but complete resorption was not seen until day 26.

Treatments of COVID-19 patients were initially started as Triple therapy: Azithromycin + Oseltamivir + Hydroxychloroquine, according to the COVID-19 treatment recommendations of the Ministry of Health of the Republic of Turkey. Treatment of patients whose clinical, radiological or laboratory deteriorated despite initial therapy was continued Quadruple therapy: Azithromycin + Oseltamivir + Hydroxychloroquine + Favipiravir and MV (Mechanical Ventilation) as needed (**Figure 2**). According to the clinical decision, 61,1% (99 patients) of the admitted patients were evaluated as COVID-19 positive and treatment were started. According to the clinical decision, 61.1% of the patients (99 patients) were evaluated as COVID-19 positive and treatment was started. Triple therapy treatment was started in 79.8% (79) of COVID-19 patients. The mean age was 52.87±18.70 (range 18-90) years and 51.5% (51) of them were male. When the treatments received by the patients were analyzed according to age groups, a significant difference was found (p=0.004). It was determined that patients over 65 years old received quadruple therapy (26.7%) and quadruple therapy+MV treatments (13.3%) more than patients under 65 years of age (**Figure 1**).

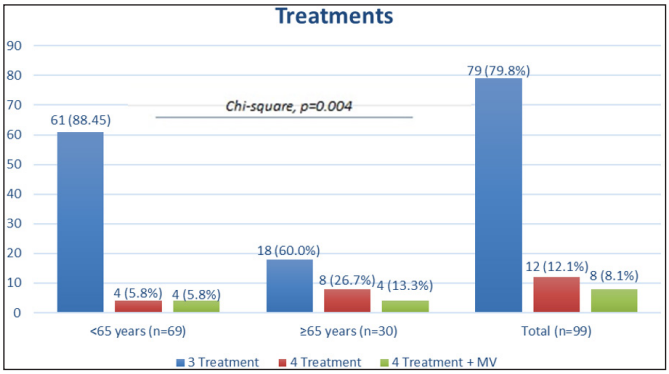

Figure 2. Treatments of COVID-19 patients Triple Treatment: Azithromycin + Oseltamivir + Hydroxychloroquine, Quad Treatment: Azithromycin + Oseltamivir + Hydroxychloroquine + Favipiravir, MV: Mechanical Ventilation).

According to the clinical decision, 57% (62 patients) of the patients were diagnosed with a true positive diagnosis by chest tomography, a true negative diagnosis was made for 39% (63 patients), and a false negative diagnosis was made for 4% (7 patients). The sensitivity (92.9%), specificity (100%), PPD (100%) and NPD I (90%), accuracy (95.7%) and kappa value (0.911) of chest tomography were found to be high. When the age groups

were evaluated separately, it was noted that the sensitivity of thorax tomography decreased to 89.9% in the group under 65 years of age (**Table 2**).

According to the clinical decision, 50% (62 patients) of 124 patients under the age of 65 years included in the study had a correct positive diagnosis by chest tomography, 44% (55 patients) had a negative diagnosis and 6% (7 patients) had a false negative diagnosis. None of the patients under 65 years of age have been diagnosed false positive by chest tomography (**Table 2**).

The compliance of chest CT with PCR test in clinical diagnosis is evaluated in **Table 3.** There were 28 patients, both of whom evaluated as COVID-19 positive, and 63 patients, which evaluated as COVID-19 negative, and the kappa value of both diagnostic methods was calculated as 0.186 (p=0.056). In **Figures 3** and **4**; the results of 162 patients who underwent PCR test and chest CT, and the treatments they received were evaluated according to the expert clinical opinion. While with chest CT 56.8%(92)of the 162 patients were diagnosed as COVID-19, with the PCR test 21.6% (35) patients were diagnosed. According to the clinical expert opinion, 78. 3% (72) of the 92 patients diagnosed with CT got triple therapy, 13% (12), quad therapy, and 8,7% (8), quad therapy and mechanical ventilation support. 40.1(51) % of 127 patients, PCR test COVID-19 negative got triple therapy, 7.1% (9) quad therapy, and 3.1(4) % quad therapy and mechanical ventilation support.

Table 2. Diagnostic value of Torax CT scan according to clinical decision

	<65 years n=124	≥65 years n=38	Total n=162
TP, n (%)	62 (50)	30 (79)	92 (57)
FP, n (%)	0	0	0
TN, n (%)	55 (44)	8 (21)	63 (39)
FN, n (%)	7 (6)	0	7 (4)
Sensitivity, %	89.9	100	92.9
Specifity, %	100	100	100
PPV, %	100	100	100
NPV, %	88.7	100	90
Accuracy, %	94.3	100	95.7
Kappavalue (p)	0.887 (p=0.041)	1.00 (p<0.001)	0.911 (p=0.033)

TP indicates true-positive; FP, false-positive; TN, true-negative; FN, false-negative
PPV: Positive Predictive Value, NPV: Negative Predictive Value

Table 3. Torax CT scan and RT-PCR consistency in diagnosis

	<65 years n=124	≥65 years n=38	Total n=162
CT + PCR +, n (%)	19 (15)	9 (24)	28 (17)
CT + PCR -, n (%)	43 (35)	21 (55)	64 (40)
CT - PCR +, n (%)	7 (6)	0	7 (4)
CT - PCR -, n (%)	55(44)	8 (21)	63 (39)
Accuracy, %	60	45	56
Kappa value (p)	0.194 (p=0.072)	0.153 (p=0.066)	0.186 (p=0.056)

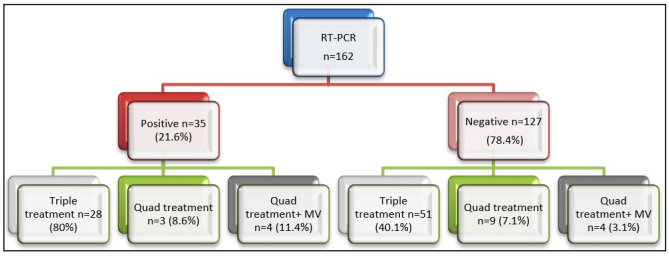

Figure 3. Treatment Distributions Based on Pcr Results. (Triple Treatment: Azithromycin + Oseltamivir + Hydroxychloroquine, Quad Treatment: Azithromycin + Oseltamivir + Hydroxychloroquine + Favipiravir, MV: Mechanical Ventilation).

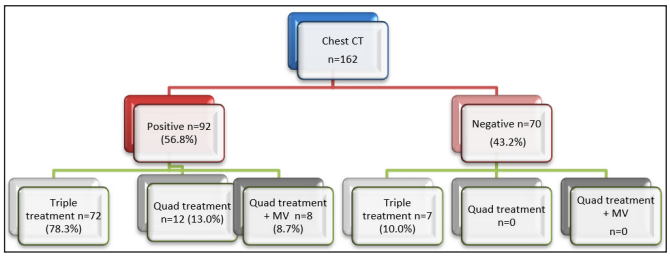

Figure 4. Treatment Distributions According to Chest CT Results. (Triple Treatment: Azithromycin + Oseltamivir + Hydroxychloroquine, Quad Treatment: Azithromycin + Oseltamivir + Hydroxychloroquine + Favipiravir, MV: Mechanical Ventilation).

DISCUSSION

Our study results showed that diagnosis can be missed with RT-PCR and chest X-ray in patients with COVID-19 pneumonia. When the diagnosis was confirmed with lung tomography in patients with high clinical suspicion, radiological findings of COVID-19 were found in patients who were falsely diagnosed with chest X-ray and RT-PCR. Early and accurate diagnosis of COVID-19 has a very important role in ensuring rapid isolation and consequently pandemic control. Also, starting the treatment of patients in a short time will contribute to the reduction of mortality. In a study conducted by Chen N et al. (11) with 99 patients, the mean age was 55,5 years and 67% of the patients were male, and the probability of infection with COVID-19 was higher in older men. In another study involving 1049 patients in China, the average age was 51 years, while 54% were reported as women (12). RT-PCR and chest CT were taken simultaneously in this study. COVID-19 suspicious patients are included. All patients with COVID-19 symptoms compatible with RT-PCR positive or chest CT compatible with viral pneumonia have been accepted as COVID-19 and treatment has been started. According to the results, the average age of patients with COVID 19 was 52,6±18.7 years, while 51.5% were male patients.

The number of patients with viral pneumonia on chest CT was 92 (56,8%) and the sensitivity of CT was found to be high with 92.9% according to the expert view. This rate was 76% in the study of Zhong et al (13). The false-negative rate of chest CT was only 7 (6%). All of these

patients received triple therapy and the clinics of patients were in good conditions. In a study conducted by Tao Ai et al. (12) in 1014 patients, the number of patients with RT-PCR positive but without CT findings in chest CT was reported as 21 (3%), while chest CT of 888 (87.5%) patients was found to be compatible with viral pneumonia. In a study in which Xingzhi Xie et al. (14) examined 167 patients, the false negativity rate of chest CT was reported as only 7 (4%) and in another study involving 99 patients, it was reported as 2%. This result may show that the number of COVID-19 patients with a mild clinical course without pneumonia is low. It can also be attributed to the high false-negative rate of RT-PCR results in this patient group. In the study conducted by Ai T et al (12), the rate of false negativity was reported as 30.8%. This may be due to the RT-PCR result being dependent on external factors such as the sampling, preservation, the stage of the disease and the reliability of the test kits. These results showed that when acting only according to the PCR result, a significant number of patients would remain untreated and would pose a major problem in terms of isolation and pandemic control. Kesmez et al (7),311 RT-PCR positive Chest CT findings of 21.9% of the patients were evaluated as normal. In our study, the rate of chest CT performed in RT-PCR positive patients was 45.7%. Chunqin Long et al (16), diagnosed a total of 36 cases of COVID-19 pneumonia. Thirty-five patients had abnormal CT findings at presentation and only one patient had a normal chest CT. 30 cases were detected positive by RT-PCR and 6 cases were initially missed. Of these 6 missed cases, 3 tested positive in the second RT-PCR test and the other 3 were positive in the third round of RT-PCR evaluations. While the sensitivity of CT scans at admission was 97.2%, the sensitivity of first-round rRT-PCR was 84.6%. In our study, the sensitivity (92.9%) and specificity (100%) of chest tomography were found. When the age groups were evaluated separately, it was noted that the sensitivity of thorax tomography decreased to 89.9% in the group under 65 years of age. In a case of Hao Feng et al (17), a 34-year-old male patient had a negative RT-PCR test on four consecutive pharyngeal swabs. Chest CT showed findings consistent with COVID-19 at admission. However, the fifth RT-PCR test gave a positive result on the fifth day after admission. It is difficult to distinguish COVID-19 pneumonia from other viral pneumonias by CT findings alone; however, they highlight the usefulness of chest CT for early detection of COVID-19 when RT-PCR tests show negative results. These results are consistent with our study, for early diagnosis and treatment, false negative RT-PCR should be kept in mind in case of clinical suspicion, and tomography should be performed when necessary. The study of Joseph V Waller et al.(18) emphasized that CT has limited sensitivity and lower specificity than RT-PCR testing for COVID-19, but the importance of Chest CT as a complementary diagnostic tool, especially in symptomatic patients. In a case series study by Eric D. Tenda et al (19); Strongly recommends the use of non-contrast chest CT to diagnose COVID-19 in patients with RT-PCR negative, chest X-ray non-diagnostic and moderate symptoms.

Chest CT showed that it has a very important tool in the diagnosis of COVID-19 with an accuracy of 95,7%. In addition, while chest CT results immediately, RT-PCR results require several hours. In a study involving 53 positive patients, 37 (69,8%) reported that early diagnosis was made with the result of thoracic CT, lung imaging findings were detected before symptoms occurred, and laboratory tests were concluded approximately 3 days later (20).

This study has some limitations. First this study was retrospective an single center. In the application, recurrent PCR results of patients who were negative for PCR were not expected, only PCR results at the time of application were evaluated. But this is also the hypothesis of this study because we advocated that simultaneous chest CT use with PCR test to the patients is a reliable and confirmatory approach, especially in order not to miss or delay the diagnosis of the patients during admission.

CONCLUSION

COVID-19 pneumonia is a serious, life-threatening condition. Rapid diagnosis and early treatment are very important in terms of reducing mortality and morbidity. In addition, early diagnosis is important for more efficient use of hospital resources. It is very important to use diagnostic methods with high sensitivity and specificity in order to reach a rapid diagnosis. Therefore, chest CT application may be appropriate in patients with clinically negative COVID-19 pneumonia, chest X-ray and RT-PCR test. Chest CT can be life-saving with early diagnosis, especially in elderly patients. Further studies with larger series are needed on this subject.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Yıldırım Beyazıt University Faculty of Medicine Clinical Research Ethics Committee (Date; 09.09.2020, Decision No: 72).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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